REMARKS

Claims 1, 2, 4, 26-34 are pending in this application. Claims 1, 2, 4, 26-29 and 32-34 have been consideration in this Office Action and stand rejected. Claims 30-31 have been withdrawn from consideration because they allegedly read on non-elected inventions and species.

Applicants thank the Examiner for considering Applicants' response to a restriction requirement filed on March 1, 2004. Applicants have amended the claims to present the claimed subject matter in clearer terms. Support for the claim amendment reciting an antibody directed to PSGL or a fragment thereof that binds PSGL is found at least at page 3, line 18 to page 4, line 1, of the substitute specification filed November 1, 2001. Additionally, Applicants have amended the independent method claims to now recite an additional step of determining that a mammalian subject would benefit from inhibition of a cytotoxic T cell activity. Support for this claim amendment can be found at least at page 34, lines 4-10 of the substitute specification. Support for new claim 35 may be found in the specification on page 6, lines 8-19 and page 34, lines 4-10. Lastly, Applicants cancel claim 33 without prejudice and reserve the right to pursue the subject matter of this claim in this or a continuation application. Accordingly, claims 1, 26-29, 32, 34, and 35 will remain pending upon the entry of this amendment and response.

Applicants respectfully request consideration and examination of this application and the timely allowance of the pending claims in view of the arguments below.

Formalities

The Examiner requires correction of all spelling, TRADEMARKS, and like errors. Applicants submit that a review of the substitute specification filed by the Applicants on

November 1, 2001, identified no spelling or trademark errors, however, Applicants kindly ask the Examiner to specify any required corrections relating to use of trademarks of which he is aware.

Enablement Rejection under 35 U.S.C. § 112, first paragraph

The Examiner has rejected claims 1, 2, 4, 26-29 and 32-34 under 35 U.S.C. § 112, first paragraph, as allegedly not being enabled by the specification as-filed. While the Examiner acknowledges that the specification is enabling for antibody fragments that bind PSGL, the Examiner alleges that the specification does not reasonably provide enablement for any "antibody fragment." *See* Office Action at 2. The Examiner further contends that not all antibody fragments will provide the appropriate specificity and functional characteristics necessary to carry out the claimed methods. *Id.* at 3.

Additionally, the Examiner's states that if the claimed "fragment thereof" is meant to modify PSGL rather than anti-PSGL antibody, then Applicants should provide a functional activity that can be measured with respect to the PSGL fragment, as not all PSGL fragments would provide the appropriate target of anti-PSGL antibodies that would lead to the inhibition of a cytotoxic activity of a T cell. Office Action at 3.

Without acquiescing to this rejection, however, to more clearly define subject matter, Applicants have amended the claims to recite an antibody directed to PSGL or a fragment thereof that binds PSGL. Accordingly, this amendment clarifies that the claimed invention is not directed to any "antibody fragment" but only those fragments of antibodies that bind PSGL, which the Examiner has acknowledged is enabled by the specification as-filed.

In view of the foregoing, Applicants submit that the pending claims as amended are fully enabled by the specification as-filed and request that this rejection be reconsidered and withdrawn.

Indefiniteness Rejection under 35 U.S.C. § 112, second paragraph

Claims 1, 2, 4, 26-29 and 32-34, have been rejected as being indefinite under 35 U.S.C. § 112, second paragraph, for allegedly failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention.

First, the Examiner contends that claims 1, 2, 4, 26-29, and 32-34 are allegedly indefinite in their recitation of "inhibiting the cytotoxic activity of a T cell" because the nature of the cytotoxic activity is allegedly ambiguous. Examiner further invites Applicants to amend the claims to recite a clear measure of the intended targeted function, such as inhibiting the differentiation of a cytotoxic T lymphocyte.

Applicants respectfully disagree with the Examiner's understanding of the claimed invention. Cytotoxicity analyses are described throughout the substitute specification, including for example at page 9, lines 10-19, which discusses using peritoneal exudates lymphocytes (PEL) for assessing cytotoxicity; page 16, lines 13-19, which discusses measuring cytotoxicity in presence or absence of a PSGL-1 antibody; page 17, lines 9-22 and page 40, lines 7-14, which further discuss cytotoxicity assays. Such assays enable identification of PSGL antibodies and fragments thereof that inhibit cytotoxic T cell response, without undue experimentation.

Second, the Examiner asserts that it is unclear whether the recitation of "fragment thereof" in the claims reads on the anti-PSGL antibodies (e.g. intended to be antigen binding fragments) or on PSGL itself or possibly both. As discussed above,

Applicants have amended the claims to recite an antibody directed to PSGL or a fragment thereof that binds PSGL. Accordingly, Applicants respectfully request that this rejection be reconsidered and withdrawn.

Anticipation Rejection under 35 U.S.C. § 102(e) over *Cummings*

Claims 1, 2, 4, 26-29 and 32-34 are rejected under 35 U.S.C. § 102(e) as allegedly being anticipated by U.S. Patent No. 6,667,036 to Cummings *et al.* ("*Cummings*").

The Examiner acknowledges that *Cummings* is silent about the inhibition of a cytotoxic T lymphocyte response. Office Action at 4. The Examiner, however, alleges that it does not appear that the claim language or limitations result in a manipulative difference in the method steps when compared to the prior art disclosure. *Id.* The Examiner further states that "merely discovering and claiming a new benefit of an old process cannot render the process again patentable." The Examiner appears to contend that inhibition of cytotoxic T cell response is an inherent property of a PSGL antagonist, by further stating that "mere recognition of latent properties in the prior art does not render nonobvious an otherwise known invention." *Id.*

A proper anticipation rejection requires that each and every limitation of the claimed invention be disclosed in a single prior art reference. Further, to serve as an anticipation reference in an inherency rejection, the reference must make clear that the missing descriptive matter is necessarily present in the thing described in the reference. *Schering Corporation v. Geneva Pharmaceuticals, Inc.*, 339 F.3d 1373, 1376 (Fed. Cir. 2003).

The instant invention is based, at least in part, on the realization that inhibition of cytotoxic T cell responses is beneficial for the treatment of autoimmune conditions. Applicants' claims, as amended, recite the additional step of determining a mammalian subject would benefit from inhibition of cytotoxic T cell response. Applicants note that not only does *Cummings* fail to teach or suggest inhibition of cytotoxic T cell response, as acknowledged by the Examiner himself, but *Cummings* also does not teach or suggest determining a mammalian subject would benefit from inhibition of cytotoxic T cell response, as recited by the amended claims.

Applicants note that *Cummings* generally discusses that criteria for assessing response to therapeutic modalities employing antibodies or carbohydrate is dictated by the specific condition. *See* col. 21, lines 25-28. Specifically, *Cummings* provides certain clinical indicia for determining effective dosage of PSGL antibodies to prevent extension of myocardial infarction, acute respiratory distress syndrome, shock (low blood pressure), stroke, and organ transplant. *Id.*, lines 25-45. Accordingly, *Cummings* discusses administration of a PSGL antibody to a subject followed by assessment of a clinical response. Applicants' claims, on the other hand, now require determining a subject would benefit from inhibition of a cytotoxic T-cell response. *Cummings* provides no teaching or suggestion of determining a mammalian subject would benefit from inhibition of cytotoxic T cell response. Accordingly, *Cummings* fails to anticipate the claimed invention, either implicitly or explicitly.

Furthermore, Applicants submit that even if administration of a PSGL antagonist to a subject inherently resulted in inhibition of a cytotoxic T cell response, as alleged by the Examiner, the additional step of determining the subject would benefit from inhibition

of the cytotoxic T cell response in Applicants' claims, is not present in the disclosure of *Cummings*, either explicitly or implicitly. Accordingly, Applicants submit that the additional determining step renders the claims both novel and unobvious in view of *Cummings*.

Anticipation Rejection under 35 U.S.C. § 102(e) over *Larsen*

Claims 1, 2, 4, 26-29 and 32-34 are rejected under 35 U.S.C. §102(e) as being allegedly anticipated by U.S. Patent No. 6,277,975 to Larsen *et al.* ("*Larsen*").

The Examiner once again acknowledges that *Larsen* is silent about inhibition of a cytotoxic T lymphocyte response. Office Action at 4. The Examiner, however, contends that it does not appear that the claim language or limitations result in a manipulative difference in the method steps when compared to the prior art disclosure. As in case of *Cummings*, the Examiner again appears to contend that inhibition of cytotoxic T cell response is an inherent property of a PSGL antagonist, by stating that "mere recognition of latent properties in the prior art does not render nonobvious an otherwise known invention." *Id.*

Applicants respectfully traverse this rejection. Applicants have amended the claims to introduce the additional step of determining a subject would benefit from inhibition of cytotoxic T cell response.

Larsen discusses use of PSGL antibodies, among other compounds which interfere with P-selectin binding, for modulating several functions relating to leukocyte adherence, inflammation, tumor metastases, and coagulation. *See* col. 18, lines 34-54. Larsen further discusses that neutralizing monoclonal antibodies to PSGL or to complex carbohydrates characteristic of PSGL may be useful therapeutics for both inflammatory

diseases and some forms of cancer where abnormal expression of PSGL is involved. *See* col. 20, lines 21-26. Applicants submit that not only does *Larsen* fail to teach or suggest inhibition of a cytotoxic T cell response, as acknowledged by the Examiner himself, but *Larsen* also does not teach or suggest determining a subject would benefit from inhibition of cytotoxic T cell response. Additionally, even if inhibition of a cytotoxic T cell response was an inherent property of a PSGL antibody, as alleged by the Examiner, determining if a patient would benefit from inhibition of a cytotoxic T cell response is not anticipated or rendered obvious by *Larsen* and is a novel step in the methods of the claimed invention.

In view of the foregoing, Applicants submit that the pending claims are not anticipated by *Larsen* and allow reconsideration and withdrawal of this rejection.

Provisional Non-Statutory Double Patenting Rejection

Claims 1-2 have been provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 43-58 of copending Application No. 09/431,979. In particular, the Examiner is contending that although the conflicting claims are not identical, they are not patentably distinct from each other because they are drawn to the same or nearly the same methods of inhibiting T cell cytotoxicity with the same or nearly the same soluble forms of PSGL. Office Action at 5.

Applicants note that this is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Applicants respectfully traverse this rejection, but, at this time, respectfully request that this rejection be held in abeyance until allowable subject matter is determined. At that time, Applicants will consider whether to file a Terminal Disclaimer.

CONCLUSION

In view of the foregoing remarks, Applicants respectfully request withdrawal of this rejection and timely allowance of the pending claims. Should the Examiner have remaining questions or concerns regarding this application, Applicants request that the Examiner contact the undersigned at 202-408-4086 to schedule an interview to discuss the application.

Please grant any extensions of time required to enter this response and charge any additional required fees to our deposit account 06-0916.

Respectfully submitted,

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Dated: September 15, 2004

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